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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/527,440	03/17/2000	Hiroki Nakae	HIRA.0003	3095

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EXAMINER

CLOW, LORI A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 09/25/2002

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/527,440	Applicant(s) NAKAE ET AL.	
	Examiner Lori A. Clow, Ph.D.	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 30-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 30-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's arguments filed 20 August 2002 have been fully considered but they are not deemed persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-4 and 30-37 are currently pending. Claims 7, 19, 20, and 22 have been cancelled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

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claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 and 30-37 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Vijg et al. (WO 98/06872; US 6,007,231) in view of Xu et al. (Genomics (1998) vol. 47, p.171-179) in further view of Harris (Genome Research (1997) vol. 7: pp.754-762).

AS stated in the previous office action, Vigj et al. (WO 98/06782; US 6,007,231) disclose the system, software, and methods for designing primers that comprise each of the recited means, and result in the selection and correlation of PCR primers with exons of DNA sequences that have been retrieved from a database. Figures 6-8 of Vijg et al. clearly identifies the means and functions disclosed in the publication, and how those means and functions are used to identify and design PCR primers (see also pages 17-19 and 23-28). Design parameters include base length, GC content etc., as well as position in relationship to an exon, sequence similarity to other sequences, etc. Vigj et al. specifically note that primers for the amplification of multiple exons from a gene can be identified, designed, and collated by the disclosed system (page 5, line 22). Applicant states that Vijg generate only one exon at a time, however, it is clear that this automated method was developed to "amplify many different exons simultaneously in the same reaction in which groups of target fragments (groups of exons) are amplified...(page 5, paragraph 3 and page 6 paragraph 1). Vigj et al. indicate that genes of varying known function

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can be analyzed, meeting all of the limitations of the instant claims except the limitation of "predicted exons". However, Xu et al. meet that limitation.

Applicant contends that Xu et al. simply utilize cDNA for identification of exon boundaries. However, as stated in the previous office action, Xu et al. teach a new experimental protocol which is able to identify exon boundaries. ExonPCR, by passes the isolation, characterization, and DNA sequencing of subclones from genomic DNA to determine exon boundaries (see abstract). More specifically, Xu et al. teach the ExonPCR algorithm, used to predict a plurality of different exons. The algorithm divides the DNA into regions of the following three types: (E) no splice site, (I) splice site, and (U) unknown. k pairs of primers are designed in the first round of PCR and later rounds subdivide each region until the desired resolution is reached (p. 175, paragraphs 1 and 2). This method relies upon the use of database queries to retrieve sequence information (p. 178, paragraph 1).

Applicant further contends that there is no mention of the selecting conditions a-d, as put forth in the instant application. However, if one reads Vigj and Xu et al. carefully it is clear the various steps are included. For example Vigj et al. disclose the steps of selecting genomic DNA from Genbank, Xu et al. disclose the prediction of exons, as outlined above. Primers are designed for the plurality of potential exons, in Vigj (column 5, line 38), and gathered as a collection corresponding to exons in a particular sequence (page 6, 2nd paragraph). Thus, Vigj and Xu do include all of the steps in the instant application.

Applicant argues that Vigj et al. do not provide the selection criteria that are provided in the instant application. However, as stated above, the design parameters include melting temperature, which inherently assesses GC content, and base length.

Finally, applicant argues that there is no establishment of a motivation to combine the teachings of Vigj et al. and Xu et al. However, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Vigj and Xu, based upon the knowledge that annotation in the field of molecular biology and bioinformatics would be a valuable tool and that combinations of already existing databases to perform the tasks proposed in the instant application would be also obvious.

While Vigj et al. and Xu et al. do not combine the various tools into one application, as does the instant invention, Harris does (Genome Research). In the program known as Genotator, developed in 1997, Harris has addressed the need to develop a tool for analyzing DNA as a whole and to incorporate various programs and databases into one system (introduction). One such advantage of this tool is that exons may be predicted and primer design implemented (abstract). "Genotator provides a flexible, transparent system for automatically running a series of sequence analysis programs on genetic sequences" (p.755, column 1). The Genotator can run several gene finder programs and perform homology searches using BLAST. It saves the results for further use. The tool is powerful in that it allows the user to modify the code in order to integrate favorite sequence analysis tools (p. 756, column 1). Primers may be selected using, for example, Primer3 analysis. Clearly, the motivation to combine the teachings of Vigj and Xu with those of Harris, are provided in the Genotator system, which virtually allows custom analysis integration for exon discovery etc.

No claim is allowed.


Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Bill Phillips, whose telephone number is (703) 305-3419, or to the Technical Center receptionist whose telephone number is (703) 308-0196.


MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

September 16, 2002

Lori A. Clow, Ph.D.
Art Unit 1631

